



TFW 1644

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/520,431-Conf. #2810
	Filing Date	July 27, 2005
	First Named Inventor	Lawrence G. Lum
	Art Unit	1644
	Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission	Attorney Docket Number	57734(11259)

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please Identify below): Notification of Transmittal of the International Search Report or the Declaration (5 pages) Notification of Transmittal of International Preliminary Examination Report (4 pages) Return Receipt Postcard
Remarks		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	EDWARDS ANGELL PALMER & DODGE LLP		
Signature	<i>Kathryn A. Piffat, Ph.D.</i>		
Printed name	Kathryn A. Piffat, Ph.D.		
Date	February 16, 2006	Reg. No.	34,901



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Application No. (if known): 10/520,431

Attorney Docket No.: 57734(11259)

Certificate of Mailing under 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

on February 16, 2006
Date

Signature

Sharon Bizokas

Typed or printed name of person signing Certificate

@@@
Registration Number, if applicable

(617) 439-4444
Telephone Number

Note: Each paper must have its own certificate of mailing, or this certificate must identify each submitted paper.

Transmittal (1 page)

Notification of Transmittal of the International Search Report or the Declaration (5 pages)

Notification of Transmittal of International Preliminary Examination Report (4 pages)

Return Receipt Postcard

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
ROBERT L. BUCHANAN
EDWARDS & ANGELL, LLP
P.O. BOX 9169
BOSTON, MA 02209

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 57734-PCT	Date of Mailing (day/month/year) 13 OCT 2004
International application No. PCT/US03/21142	International filing date (day/month/year) 03 July 2003 (03.07.2003)
Applicant ROGER WILLIAMS MEDICAL CENTER	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 bis.1 and 90 bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <i>Michael A Belyavskyi</i> Michael A Belyavskyi Telephone No. 571-272-1600
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 57734-PCT	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US03/21142	International filing date (<i>day/month/year</i>) 03 July 2003 (03.07.2003)	(Earliest) Priority Date (<i>day/month/year</i>) 05 July 2002 (05.07.2002)
Applicant ROGER WILLIAMS MEDICAL CENTER		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/21142

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/395; A01N 63/00; A61K 35/26, 35/28

US CL : 424/136.1, 153.1, 155.1, 93.7, 577

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/136.1, 153.1, 155.1, 93.7, 577

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SEN, M. et al Cutting Edge Communication: Use of antiCD3+ anti-HER2 bispecific antibody for Redirecting Cytotoxicity of Activated T Cells Toward HER2/neu + Tumors. Journal of Hematotherapy. 2001, Vol. 10, No. 2, pages 247-260, see entire document.	1-54
Y	TREVOR, K. et al. Bispecific Antibody Reactivation of Gene-Transduced T Cell: Implications for Cancer Immunotherapy and Gene Therapy. Tumor Targeting. 2000, Vol. 4, No. 4, pages 245-256, see entire document.	1-54
A	WO 03/091398 A2 (ROGER WILLIAMS HOSPITAL) 06 November 2003 (06.11.2003).	1-54
Y	US 6,010,902 A (LEDBETTER et al) 04 January 2000(04.01.2000), see entire document.	1-54
A	WO 03/090513 A2 (ROGER WILLIAMS HOSPITAL) 06 November 2003 (06.11.2003) see entire document, Abstract in particular.	1-54
Y,P	WO 03/015705 A2 (ROGER WILLIAMS HOSPITAL) 27 February 2003 (27.02.2003).	1-54

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

18 August 2004 (18.08.2004)

Date of mailing of the international search report

13 OCT 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Michael A Belyavsky
Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

PCT/US03/21142

Continuation of B. FIELDS SEARCHED Item 3:

BIOSIS, CAPLUS, SCISEARCH, MEDLINE, EMBASE, USPATFULL, PCTFULL, WEST

Search terms: applicants name, tracking cell, heteroconjugated, bispecific antibody, stem cell, arming, cancer, labeled, redirecting

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled; no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

DGC/KAP <7734-WO (11259)

PATENT COOPERATION TREATY

NOTED ON SYSTEM

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
ROBERT L. BUCHANAN
EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

RECEIVED

DEC 19 2005

EDWARDS ANGELL PALMER & DODGE LLP
IPEA/COMETINE DEPT. 1203

PCT

NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing
(day/month/year)

15 DEC 2005

Applicant's or agent's file reference

57734-PCT

IMPORTANT NOTIFICATION

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US03/21142

03 July 2003 (03.07.2003)

05 July 2002 (05.07.2002)

Applicant

ROGER WILLIAMS MEDICAL CENTER

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Mail Stop PCT, Attn: IPEA/ US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Michail A. Belyavskiy

Telephone No. 571-272-1600

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 57734-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/21142	International filing date (day/month/year) 03 July 2003 (03.07.2003)	Priority date (day/month/year) 05 July 2002 (05.07.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 39/395; A01N 63/00; A61K 35/26,35/28 and US Cl.: 424/136.1, 153.1,155.1,93.7,577		
Applicant ROGER WILLIAMS MEDICAL CENTER		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>—</u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 03 February 2004 (03.02.2004)	Date of completion of this report 12 September 2005 (12.09.2005)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Michail A. Belyavskyi Telephone No. 571-272-1600	

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/21142

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-67 _____ as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the claims:
pages 68-75 _____, as originally filed
pages NONE _____, as amended (together with any statement) under Article 19
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the drawings:
pages 1-9 _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages none
- ☒ the claims, Nos. none
- ☒ the drawings, sheets/fig none

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/21142

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>1-14 and 26-54</u>	YES
	Claims <u>15-25</u>	NO
Inventive Step (IS)	Claims <u>1-14</u>	YES
	Claims <u>15-54</u>	NO
Industrial Applicability (IA)	Claims <u>1-54</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 15-25 lack novelty under PCT Article 33(2) as being anticipated by Sen et al. Sen et al., teach a method of treating a patient suffering from cancer comprising isolating peripheral blood mononuclear cells from a patient suffering from cancer, activating T cells by ex-vivo stimulating with anti-CD3 monoclonal antibody and arming activated T cells with bispecific antibodies binding the secondary labeled antibody specific for the Fc region of the bispecific antibody and reinfusing the armed and labeled activated T cell into the patient (see entire document, Material and Method, pages 257, and 258 in particular).

The reference teaching anticipated the claimed invention.

Claims 26-54 lack an inventive step under PCT Article 33(3) as being obvious over Sen et al.

The teaching of Sen et al. have being discussed supra.

Sen et al., do not teach a method for tracking cells in vivo at any desired location. However, said functional properties would be an obvious variation of the method taught by Sen et al.

Claims 1-14 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed invention as recited in claims 1-14.